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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/758,798 | 01/16/2004 | Stanley J. Wiegand | REG 980A | 6501 |

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| EXAMINER | |
|---|---|
| LOCKARD, JON MCCLELLAND | |
| ART UNIT | PAPER NUMBER |
| 1647 | |

DATE MAILED: 04/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/758,798 | WIEGAND ET AL. | |
| | Examiner | Art Unit | |
| | Jon M. Lockard | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *6-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/16/04, 10/21/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election of Group III, claims 6-13, drawn to a method for inhibiting pain or nociception comprising administering a therapeutically effective amount of a first agent capable of modulating NMUR2 activity, in the reply filed on 17 January 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-5 and 14-16 have been cancelled. Therefore, claims 6-13, as they read upon the elected species of chronic pain resulting from injury to the body, are pending and the subject of this Office Action.

### *Information Disclosure Statement*

3. The information disclosure statements (IDS) submitted on 01 January 2004 and 21 October 2004 have been considered by the examiner.

### *Specification*

4. The disclosure is objected to because of the following informalities:

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

6. Patent applications are referenced in the disclosure (pg 4, line 5). The status of the applications must be updated.

### *Claim Objections*

7. Claim 13 is objected to because of the following informalities: Claim 13 encompasses non-elected inventions, e.g., chronic fatigue syndrome and fibromyalgia. Appropriate correction is suggested.

### *Claim Rejections - 35 USC § 112, 1st Paragraph (Scope of Enablement)*

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 6-9 and 11-13 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method of inhibiting pain or nociception comprising administering an agent capable of modulating NMUR2 activity, wherein the agent is an antibody which binds the neuromedin U receptor 2 (NMUR2), does not reasonably provide enablement for a method of inhibiting pain or nociception comprising administering any agent capable of modulating NMUR2 activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

10. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level

of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

11. The claims are drawn very broadly to a first agent that is capable of modulating NMUR2 activity. While the specification provides adequate guidance for the skilled artisan to make and use antibodies which bind the NMUR2 receptor in the claimed methods (See pg 3 [0009]-[0011]), it does not provide adequate guidance for a commensurate number of the claimed species of agents which are capable of modulating NMUR2 activity, which the specification teaches can be an antibody which binds neuromedin U (NMU), carbohydrates, lipids, proteins, peptides, peptidomimetics, nucleic acids, small molecules, and other drugs (See pg 6 [0026]). Based on the very limited number of disclosed species, it is not at all predictable what essential structural features are required for a compound to have the claimed property of being a modulator of NMUR2 activity, and it would require undue experimentation to determine such. Furthermore, given the pleiotropic effects of neuromedin U, it is unpredictable what effects administering an antibody which binds neuromedin U would have on a subject (See for example Brighton et al. (2004). Neuromedin U and its receptors: structure, function, and physiological roles. Pharmacological Reviews. 56(2):231-248). Lastly, claims 6-8 and 12-13 do not even require that that compound inhibits the activity of NMUR2, which, based on the teachings of the Specification, would not produce the desired effect of inhibiting pain or nociception. As the specification does not teach how to make and use a number of species that would be commensurate in scope with the claims, one skilled in the art would require undue

experimentation to practice the invention in a manner commensurate in scope with the claims, given the lack of guidance in the specification and the very broad scope of the claims.

12. Due to the large quantity of experimentation necessary to generate the infinite number of agents that are capable of modulating NMUR2 activity recited in the claims; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide binding/activity of the antagonist; and the breadth of the claims which fail to recite any structural or functional limitations; it would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to make and/or use the Applicants' invention in its full scope.

***Claim Rejections - 35 USC § 112, 1st Paragraph (Written Description)***

13. Claims 6-9 and 11-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

14. The claims are drawn very broadly to a first agent that is capable of modulating NMUR2 activity. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or

chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claims is a desired functional property in the form of the recitation of modulating NMUR2 activity. However, there does not appear to be an adequate written description in the specification as filed of any essential structural feature common to molecules that are modulators of NMUR2 activity. While the specification provides adequate written description for antibodies which bind the NMUR2 receptor, it does not provide adequate written description for a commensurate number of the claimed species of agents which are capable of modulating NMUR2 activity, which the specification teaches can be an antibody which binds neuromedin U (NMU), carbohydrates, lipids, proteins, peptides, peptidomimetics, nucleic acids, small molecules, and other drugs (See pg 6 [0026]). The distinguishing characteristics of the claimed genus are not described. The only adequately described species are the antibodies which bind to NMUR2. Accordingly, the specification does not provide adequate written description of the claimed genus.

15. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

16. With the exception of the NMUR2 antibodies referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed NMUR2 modulators, and therefore

conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The product itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

17. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

18. Therefore, only antibodies which bind NMUR2, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

***Claim Rejections - 35 USC § 112***

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claims 6-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

21. Claim 6 is rejected as being indefinite because it recites the abbreviation NMUR2, which should be spelled out in all independent claims in the interest of clarity. The mere recitation of an acronym is insufficient to indicate the metes and bounds of the claim, and it is suggested that the term be spelled out at its first use and identified by sufficient structural and/or functional language (i.e., SEQ ID NO:) to overcome this rejection.

22. Claim 6 is rejected as being indefinite because the claim does not have a step that clearly relates back to the preamble. For example, there is no step indicating that administration of the agent results in inhibiting pain or nociception.

23. Claim 10 recites the limitation "wherein the antagonist". There is insufficient antecedent basis for this limitation in the claim. Claim 7, from which claim 10 depends, does not recite an "antagonist".

24. Claim 11 recites the limitation "wherein the antibody". There is insufficient antecedent basis for this limitation in the claim. Claim 9, from which claim 11 depends, does not recite an "antibody".

25. Claim 12 recites the limitation "wherein the NMUR2-associated condition". There is insufficient antecedent basis for this limitation in the claim. Claim 6, from which claim 12 depends, does not recite an "NMUR2-associated condition".

26. Claim 12 is rejected as being indefinite for reciting the term "NMUR2-associated condition". Since neither the art nor the specification provides an unambiguous definition of the term, the metes and bounds of the claim cannot be determined.

27. Claims 7-9 and 13 are rejected for depending from an indefinite claim.

*Claim Rejections - 35 USC § 102*

28. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

29. Claims 6 and 9-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Elshourbagy et al. (U.S. Pat. No. 6,461,836, filed 10 April 2000).

30. Elshourbagy et al. teach a neuromedin U receptor 2 (NMUR2) (See SEQ ID NO:2) as well as ligands U-8, U-25, and U-23 that bind to it. Elshourbagy et al. also teach that antibodies to the receptor protein may be employed to treat diseases of the invention (See column 11, lines 43-45), which include pain (See column 3, line 3). Elshourbagy et al. also teach that the antibodies can include monoclonal antibodies, single chain antibodies, and humanized antibodies (See column 11, lines 14-40). It is noted that the recitation in claim 6 (and claims dependent thereof) of "A therapeutic method for inhibiting pain or nociception" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152,

88 USPQ 478, 481 (CCPA 1951). Thus, Elshourbagy et al. meets all the limitations of claims 6 and 9-13.

***Claim Rejections - 35 USC § 103***

31. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

32. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

33. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elshourbagy et al. as applied to claims 6 and 9-13 above, and further in view of Zhorov et al. (U.S. Pat. No. 4,389,404).

34. The reference of Elshourbagy et al. is summarized above.

35. The reference of Elshourbagy et al. does not teach the co-administration of NMUR2 antibodies and a second pain-reducing agent, such as morphine.

36. However, the use of morphine to treat pain was known and was routinely used in the art at the time of the invention (See for example Zhorov et al. U.S. Pat. No. 4,389,404).

37. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make and use a composition combining antibodies to NMUR2 and morphine because the molecules are taught individually to be effective for treating pain. *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

> "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art."

38. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

***Summary***

39. No claim is allowed.

40. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Yu et al. (2003). Pro-nociceptive effects of neuromedin U in rat. Neuroscience. 120:467-474.

Nakahara et al. (2004). Neuromedin U is involved in nociceptive reflexes and adaptation to environmental stimuli in mice. Biochemical and Biophysical Research Communications. 323:615-620.

*Advisory Information*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Jon M. Lockard, Ph.D.
April 8, 2006

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER